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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004			EXAMINER TRUONG, TAMTHOM NGO	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/502,538

Applicant(s)

HENNEQUIN, LAURENT
FRANCOIS ANDRE

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-20 and 22-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-20, 22-24, and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3-24-05</u> | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

Applicant's amendment of 9-30-05 has been fully considered. The amended claims and argument have overcome the previous rejection of 112/2nd paragraph, items (a)-(f), (h), (j) and (k), but the argument has not overcome the previous rejection of 112/2nd paragraph, items (g), (i) and (l). Thus, some items of the previous 112/2nd rejection are maintained herein.

Claim 21 has been cancelled, and thus, overcome the previous rejection of 101 (use claim). Said rejection is withdrawn herein.

Applicant's argument and new claim 27 have not overcome the previous rejection of 102(b) and 103 based on **Hennequin et. al.** (WO'212), and thus, those rejections are maintained herein.

Applicant has not filed a terminal disclaimer; therefore, the previous rejection of Obviousness Double Patenting is also maintained herein.

Claims 1 and 21 are cancelled.

Claims 2-20 and 22-27 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2-13, 18-20, 22 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 27 still recites the phrase “*or R¹ may be selected from any of the groups defined herein for R¹*”. Although said limitation includes the phrase “*for R¹*”, said limitation still has indefinite metes and bounds because R¹ has an extensive definition with a proviso, so it is not clear if said phrase allows R¹ to be any group with or without the proviso. Also, the phrase seems to suggest R¹ could be a combination of any of the recited groups. Therefore, the scope of R¹ is really unclear.
- b. The limitation of R² as “*6,7-methylenedioxy or 6,7-ethylenedioxy*” seems to suggest a ring. However, a ring could only be formed by two R², and not just one.
- c. Claim 19 lacks antecedent basis because it depends on claim 27 for a compound of formula I. However, process (d) recites a compound of formula I wherein R⁵ is C₁-alkylR¹¹³, and R¹¹³ is defined in terms of R¹¹⁴, R¹¹⁵, R¹¹⁶, R¹¹⁷, etc. None of those variables are recited in claim 27. Same with process (e), which recites (R²)_m represented by -NR¹²⁷R¹²⁸, which is not recited in claim 27.
- d. Claim 22 still recites “*A method for producing an antiangiogenic and/or vascular permeability reducing effect...*” Although applicant cites the intended diseases listed in the specification for such an effect, said method still has indefinite metes and bounds because the list is not limiting, and cites diseases that are examples of angiogenesis and/or increase vascular permeability. Thus, it is unclear what treatment of other

diseases is intended by the claimed method. Furthermore, the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. The test for determining complicity with 35 USC 112/2nd is whether applicants have clearly defined “their” invention not what may be discovered by future research, as this type of claim language clearly requires.

e. Claims 5 recite the term “*azaindole*” still has indefinite metes and bounds despite the definition in the specification. The definition of “*azaindole*” only provides one example of 7-*azaindole*. However, said definition also includes “similar groups”. It is not clearly what constitutes “similar groups”, and how many nitrogen atoms are in such a ring.

f. Claims 2-13, 18-20 and 22 are (also) rejected as being dependent on claim 27, and carrying out the indefinite limitations.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 1010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

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ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 2-4, 10, 18-22 and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 21-24 of copending Application No. 10/494,137. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reason stated in the previous office action.

3. Claims 2-4, 10, 18-22 and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 and 22-25 of copending Application No. 10/494,388. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reason stated in the previous office action.

4. Claims 4, 18-22 and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/344,678. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reason stated in the previous office action.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2-10, 18-22 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by **Hennequin et. al.** (WO 00/47212).

On pages 54-58, Hennequin et. al. disclose several quinazoline compounds that are substituted with *indolyl-oxy* at the 4th position, and also substituted with a group such as: 3-*(pyrrolidin-1-yl)propoxy* or 3-*piperidinopropoxy*, etc. (e.g., see **compounds on lines 30 & 31 on page 57**). Also, on page 115, Table I lists **compounds #25, 26** which are quinazoline substituted with *indazolyl-amino*;

The disclosed compounds read on the instant Formula I when it has the following substituents:

- Z is -O-, -NH-;
- Ring C is indolyl or indazolyl;
- m = 2;
- one of R² is methoxy, and the other is Q¹-X¹;
- X¹ is -O-;
- Q¹ is C₁₋₅alkylQ²;

- Q^2 is a 5- or 6-membered saturated or partially saturated heterocyclic group with 1-2 heteroatoms.

The disclosed compounds also reduce antiangiogenic effect or vascular permeability.

Note, the proviso in the definition of R^1 does not exclude the above compounds because the proviso only requires **either** R^1 or R^2 to represent one of the five groups: (i) Q^1-X^1 , (ii) $Q^{15}W^3$, (iii) $Q^{21}W^4C_{1-5}alkylX^1$, (iv) $Q^{28}C_{1-5}alkylX^1 \dots$, (v) $Q^{29}C_{1-5}alkylX^1 \dots$ etc. Thus, in the instant case the disclosed compounds read on those of Formula I wherein one of R^2 substituents is Q^1-X^1 . **Contrary to applicant's remark, the proviso in the original claim 1 and new claim 27 has already been taken into account.**

The process for making said compounds in WO'212 also reads on the process in the instant claim 19 because the same intermediates are used (see pages 66-79). For example, the disclosed Formula (III) corresponds to the instant Formula (III), and the disclosed Formula (IV) corresponds to the instant Formula (IV), etc.

Thus, the teaching of Hennequin et. al. completely anticipates the above claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 5-13, 14-17, 23, 24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Hennequin et. al.** (WO'212).

The instant claims 5-13 recite quinazoline compounds having ring C as an "*azaindolyl*". Although there is no species in WO'212 has such a ring, on page 12, Hennequin describes a preferred embodiment for ring C which includes a "*9-10-membered heteroaromatic bicyclic moiety which contains 1 or 2 nitrogen atoms.*" Such a teaching would have motivated one skilled in the art to select the instant azaindole as ring C since it met the description of the preferred embodiment.

The instant claims 14-17, 23 and 24 recite species of quinazoline compounds with indolyl-oxy and a substituent such as: *(4-acetylpiperazin-1-yl)propoxy*; *benzyloxy*; or *hydroxyl*. Although WO'212 does not appear to disclose said species, the definition of R² allows for such a substituent (e.g, page 3, line 19 (for hydroxyl), line 21 (for R⁵X¹), etc.).

Note, the proviso in claim 27 does **not** exclude the compounds or generic teaching of Hennequin et. al. which provides equivalent teaching and motivation for one skilled in the art to select *azaindolyl* as a ring represented by ring C.

Since Hennequin's compounds have the same activity, one of the ordinary skill in the art would have been motivated to select the instant species from the genus in WO'212 because said compounds would have expected to reduce antiangiogenic effect and/or vascular permeability as well.

Therefore, at the time of the invention, it would have been obvious to make and use species claimed herein in view of the teaching above.

Allowable Subject Matter

7. Claims 25 and 26 are free of prior arts. The prior art of record (cited on PTO-892) do not teach or fairly suggest a process of making 5-bromo-7-azaindole with the steps as outlines in claim 25, and the proportions recited in claim 26.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Tamthom N. Truong
Examiner
Art Unit 1624

12-20-05


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